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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,630	10/31/2003	Thomas C. Evans	NEB-211-US	3372

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HARRIET M. STRIMPEL; NEW ENGLAND BIOLABS, INC.
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EXAMINER

PAGE, BRENT T

ART UNIT	PAPER NUMBER
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1638

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05/30/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/698,630	Applicant(s) EVANS ET AL.	
	Examiner Brent Page	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-19 and 21-43 is/are pending in the application.
- 4a) Of the above claim(s) 23,24,27-31,33-37 and 40-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-19,21,22,25,26,32,38 and 39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Reply filed on 03/05/2007 by Applicant is acknowledged. Any rejection not addressed in the office action set forth below is considered hereby withdrawn.

Claim Rejections - 35 USC § 112

Claims 1, 4-19, 21-22, 25-26, 32, and 38-39 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of Avocado sunblotch viroid CLS, does not reasonably provide enablement for any CLS having "substantial homology" to Avocado sunblotch viroid or any CLS having "substantial homology" with any other viroid as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are rejected for the reasons of record on pages 3-5 of the office action mailed 09/19/2006.

Applicant's arguments filed 03/05/2007 have been fully considered but they are not persuasive.

Applicants urge that at least 3 different viroids are described with CLS in the examples and that their ability to replicate in the chloroplast had previously been established (response filed 03/05/2007 page 10).

This is not persuasive, because the Examiner pointed out the 3 examples of CLS' in the previous office action and cited peer-reviewed articles supporting the

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unpredictability of RNA localization sequences. Three examples of specific sequences as CLS's does not enable one to use any CLS having substantial homology to any part of any viroid or even any part of a specific viroid as a CLS as stated in the previous office action. There are literally millions of embodiments that are possible, and the guidance is not present in the specification to determine which of the embodiments would be functional. Additionally, the ability of the viroid to replicate in the chloroplasts was not challenged in the previous office action and does not relate the enablement rejection of record and as a claim amendment does not alter the broad language that encompasses millions of embodiments.

Applicants also urge that a novel aspect of the claimed invention resides in the use of a cleavage-deficient viroid sequence containing a CLS fused to non-viroid sequences and that a method of inactivating the self-cleaving property is described in the specification (response filed 03/05/2007 pages 10-11).

This is not persuasive because it is necessary for Applicants to claim what they believe to be novel rather than rely on the specification. The claims are not currently limited to what Applicants submit is novel.

Applicants urge that DNA can be introduced into plant cells by any number of methods (response filed 03/05/2007 page 11).

This is not persuasive because the previous office action was addressed to the unpredictability of RNA localization to the chloroplast and was not directed to transformation.

Applicants urge that they have described the introduction of DNA into the cell, transcription into RNA and then transportation to the chloroplast by way of a chaperone (CLS) (response filed 03/05/2007 page 11).

This is not persuasive because the previous office action was addressing the state of the art of localization signals for RNA to show the unpredictable nature of the sequences in relation to function, and that, therefore, Applicants were not enabled for the millions of claimed sequences as CLS's as broadly claimed. Crofts et al (2004 Plant Physiology 136: 3414-3419) state "To date, no general consensus sequences have been identified for RNA localization signals, and it is widely believed that the targeting process is likely to be more complex than first anticipated, with constant reorganization of the mRNA-protein complex en route to its final destination" (see page 3415 first column second half of third paragraph). Okita et al further address specifically, the targeting of mRNAs to organelles, specifically those of mitochondria and chloroplasts, and disclose that although RNAs are imported into the chloroplasts it is currently unclear whether the targeting is a result of specific sequence signals, localized protection of RNAs and/or the selective degradation of RNAs that are localized in the cytoplasm (see page 555 first column, last paragraph for example).

Finally, Applicants urge that the cited reference does not discuss RNA localization that is transcribed from externally introduced DNA nor localization of viroid RNA and does not include a discussion chloroplast localization sequences in viroids response filed 03/05/2007, page 11-12.

This is not persuasive because it is not necessary to establish unpredictability in each facet of the invention, especially where the art is silent. Rather, unpredictability has been demonstrated in localization signals of RNA as re-stated above by Okita et al and Crofts et al. The instant application is claiming multitudes of localization signals as part of the invention. The unpredictability demonstrated necessarily applies absent evidence to the contrary.

For the reasons stated above, the claims remain rejected under 35 USC 112 first paragraph for lacking enablement.

Claims 1, 4-19, 21-22, 25-26, 32, and 38-39 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed 03/05/2007 have been fully considered but they are not persuasive.

Applicants urge that at least 3 representative members of examples have been provided and provide an adequate written description.

This is not persuasive because Applicants currently claim any CLS having substantial homology with a viroid sequence, or consisting of "at least part" or a viroid sequence. Regardless of the properties of the described viroid being limited to chloroplast replicating viroids, there are still literally millions of embodiments with no

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guidance as to which sequences are likely to retain function as a chloroplast localization sequence. Applicants has not described the full scope of structures responsible for the function of chloroplast localization.

Applicants additionally urge that Applicants have described how to transform plant cells with DNA:

Page 7 of the previous office action states "given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming...". The reference to transformation of sequence is simply one example of the use of a sequence. The statement is more particularly referring to the fact that in the claims are multitudes of sequences that have not been described, and as the sequences have not been described, then a use of the particular sequences also could not have been described. The office action was not referring to the state of art of transforming plants with DNA in general.

Claims 1, 4-19, 21-22, 25-26, 32 and 38-39 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims contain subject matter or depend from claims that contain subject matter that was not present in the specification or claims prior to Applicant's response on 03/05/2007.

Claims 1 and 32 both recite "chloroplast-replicating" which does not contain support in the specification, therefore Claims 1 and 32 are directed to New Matter.

The dependent claims contain the same limitations and are therefore also directed to New Matter. Applicant is required to delete New Matter.

Additionally, claims 1 and 32 both recite "cleavage-inactivated viroid". This is a different scope than the closest basis for support which is located on pages 24-27 of the specification where "self-cleavage inactivated" is mentioned. This does not support the scope of inactivation for all cleavage.

The dependent claims contain the same limitations and are therefore also directed to New Matter. Applicant is required to delete New Matter.

Claim Rejections - 35 USC § 102

Claims 1, 4-14, 17-19, 21, 25-26, and 38-39 remain rejected under 35 U.S.C. 102(e) as being anticipated by Waterhouse et al for the reasons of record on pages 8-9 of the previous office action.

Applicant's arguments filed 03/05/2007 have been fully considered but they are not persuasive.

Applicants urge that the above reference describes targeting target-specific RNA to the nucleus not the chloroplast and utilizes self-splicing ribozymes.

This is not persuasive because the Examiner has pointed out that the reference also teaches a vector comprising an avocado sunblotch viroid which would inherently

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have a CLS sequence which would also then localize some of the transcribed RNA to the chloroplast.

Applicant further urges that there is no suggestion that the transcribed RNA was a cleavage-inactivated viroid sequence.

This is not persuasive because the claims as written are not limited to DNA sequences that transcribe cleavage-inactivated viroids sequences, but, in fact, encompass sequences that merely have "homology" with such a sequence, or consist of "at least part" of such a sequence. The sequence does not have to contain cleavage-inactivated viroid sequence in order to function as a CLS within the scope of the claims. The difference between the two sequences is structural and is not sequence dependent, and therefore the non-cleavage-inactivated sequences would inherently have homology to the cleavage-inactivated sequences.

Applicants finally urge that the present claimed invention differs from the art cited above in that it relies on a CLS having substantial homology with a cleavage-inactivated viroid sequence or consisting of at least part of a chloroplast replicating cleavage-inactivated viroid sequence fused to a second non-viroid sequenced.

This is not persuasive because as discussed above and in the prior office action, the CLS contained in the Avocado sunblotch viroid described by Waterhouse et al would, in fact have substantial homology with the sequences described by Applicant.

Based on the previous office action and the reasoning set forth above, the claims remain rejected under 35 USC 102(e) as being anticipated by Waterhouse et al.

Claim Rejections - 35 USC § 103

Claims 1, 4-19, 21-22, 25-26 and 38-39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Waterhouse et al in view of Sanford et al for the reasons stated on pages 10-11 of the previous office action.

Applicant's arguments filed 03/05/2007 have been fully considered but they are not persuasive.

Applicant urges that Waterhouse teaches away from the claimed invention for the reasons addressed stated above and that the combination of Waterhouse with Sanford et al does not suggest or teach the claimed invention.

This is not persuasive because the above reasoning shows that Waterhouse et al does not, in fact teach away from the present claims, and a mere assertion by Applicant that the combination of Waterhouse with Sanford et al does not suggest or teach the claimed invention is insufficient to overcome the cited art and rejections set forth in the previous office action.

Based on the previous office action and the reasoning set forth above, the claims remain rejected under 35 USC 103(a) as being unpatentable over Waterhouse et al in view of Sanford et al.

Claim 32 is free of the prior art given the failure of the prior art to teach or reasonably suggest the above method wherein the second RNA sequence is expressed as protein in the chloroplast.

No Claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brent Page whose telephone number is (514)-272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brent T Page

[Signature]
 ANNE E. HAZELIK, PH.D.
 PRIMARY E. SIGNER